Complete Summary

GUIDELINE TITLE

1) General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). 2) Update: recommendations from the Advisory Committee on Immunization Practices (ACIP) regarding administration of combination MMRV vaccine.

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices (ACIP). Update: recommendations from the Advisory Committee on Immunization Practices (ACIP) regarding administration of combination MMRV vaccine. MMWR Morb Mortal Wkly Rep 2008 Mar 14;57(10):258-60. PubMed

Kroger AT, Atkinson WL, Marcuse EK, Pickering LK, Advisory Committee on Immunization Practices (ACIP) Centers for Disease. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP) [published errata appear in MMWR Morb Mortal Wkly Rep 2007 Mar 23;56(11):256]. MMWR Recomm Rep 2006 Dec 1;55(RR-15):1-48. [202 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Kroger AT, Atkinson WL, Marcuse EK, Pickering LK, Advisory Committee on Immunization Practices (ACIP) Centers for Disease. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP) [published errata appear in MMWR Morb Mortal Wkly Rep 2007 Mar 23;56(11):256]. MMWR Recomm Rep 2006 Dec 1;55(RR-15):1-48.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- June 15, 2007, RotaTeq (Rotavirus, Live, Oral, Pentavalent Vaccine): Changes to the ADVERSE REACTIONS and POST-MARKETING sections of the product's prescribing information. The ADVERSE REACTIONS section was updated to include six cases of Kawasaki disease that were observed during the Phase 3 clinical trial.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Vaccine-preventable diseases, including the following:

- Diphtheria
- Haemophilus influenzae infection
- Hepatitis A and B
- Herpes zoster
- Human papillomavirus (HPV) infection
- Influenza
- Measles
- Meningococcal disease
- Mumps
- Pertussis
- Pneumococcal infection
- Polio
- Rotavirus (RV) infection
- Rubella
- Tetanus
- Varicella (chickenpox)

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

2006 Guideline

To provide technical guidance regarding common immunization concerns for health-care providers who administer vaccines to infants, children, adolescents, and adults

2008 Addendum

To provide updated recommendations regarding the administration of the combination measles, mumps, rubella, and varicella (MMRV) vaccine

TARGET POPULATION

Infants, children, adolescents and adults residing in the United States (including internationally adopted children and those with other special situations [e.g., pregnancy, altered immunocompetence, blood disorders])

INTERVENTIONS AND PRACTICES CONSIDERED

Immunization Practices

1. Timing and spacing of immunobiologics, including the following considerations:
    - Vaccine scheduling
    - Spacing of multiple doses of the same antigen
    - Simultaneous administration of vaccines
    - Nonsimultaneous administration of vaccines
    - Spacing of antibody-containing products and vaccines
    - Interchangeability of vaccines from different manufacturers
    - Managing lapsed vaccination schedules
    - Managing unknown or uncertain vaccination status
2. Recognizing true and untrue contraindications and precautions to vaccine administration
3. Vaccine administration
    - Infection control and sterile technique
    - Injection route and injection site
    - Intramuscular injections and needle length
    - Subcutaneous injections
    - Multiple vaccinations
    - Use of jet injectors
    - Methods for alleviating discomfort and pain associated with vaccination
    - Use of nonstandard vaccination practices

    - Preventing adverse reactions
    - Managing acute vaccine reactions
    - Implementing and enforcing occupational safety regulations
4. Storing and handling of immunobiologics
5. Managing special situations
    - Vaccination of persons with altered immunocompetence, including recipients of hematopoietic stem cell transplant
    - Concurrent administration of antimicrobial agents and vaccines
    - Tuberculosis screening and skin test reactivity
    - Severe allergy to vaccine components
    - Latex allergy
    - Vaccination of preterm infants
    - Vaccination during breast-feeding
    - Vaccination during pregnancy
    - Vaccination of persons vaccinated outside the United States, including internationally adopted children
    - Vaccination of persons with bleeding disorders and persons receiving anticoagulant therapy
6. Maintaining vaccination records and registries
7. Reporting adverse events after vaccination (e.g., Vaccine Injury Compensation Program, benefit and risk communication)
8. Adhering to standard vaccination programs to increase vaccination coverage

MAJOR OUTCOMES CONSIDERED

- Development of adequate and persisting antibody response (seroconversion rates)
- Adverse effects of vaccines
- Potency of vaccines
- Risk for occurrence of vaccine-preventable diseases

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

2008 Addendum

On February 27, 2008, new information was presented to the Advisory Committee on Immunization Practices (ACIP) regarding the risk for febrile seizures among children aged 12 to 23 months after administration of the combination measles, mumps, rubella, and varicella (MMRV) vaccine (ProQuad®, Merck & Co., Inc., Whitehouse Station, New Jersey). At this meeting, ACIP considered the preliminary results from the Vaccine Safety Datalink (VSD) and Merck studies, which suggested an increased risk for febrile seizures after the first dose of MMRV vaccine. Given the availability of alternative options for vaccination against measles, mumps, rubella, and varicella and the limited supply of MMRV vaccine, ACIP voted to change the preference language for MMRV vaccine to read as follows: "Combination MMRV vaccine is approved for use among healthy children aged 12 months to 12 years. MMRV vaccine is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella. ACIP does not express a preference for use of MMRV vaccine over separate injections of equivalent component vaccines (i.e., MMR vaccine and varicella vaccine)."

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

2008 Addendum

On February 27, 2008, new information was presented to the Advisory Committee on Immunization Practices (ACIP) regarding the risk for febrile seizures among children aged 12--23 months after administration of the combination measles, mumps, rubella, and varicella (MMRV) vaccine (ProQuad®, Merck & Co., Inc., Whitehouse Station, New Jersey). The original addendum document summarizes current knowledge regarding the risk for febrile seizures after MMRV vaccination and presents updated ACIP recommendations that were issued after presentation of the new information. These updated recommendations remove ACIP's previous preference for administering combination MMRV vaccine over separate injections of equivalent component vaccines (i.e., measles, mumps, and rubella [MMR] vaccine and varicella vaccine).

The combination tetravalent MMRV vaccine was licensed by the Food and Drug Administration (FDA) on September 6, 2005, for use in children aged 12 months to 12 years. MMRV vaccine can be used in place of trivalent MMR vaccine and monovalent varicella vaccine to implement the recommended 2-dose vaccine policies for prevention of measles, mumps, rubella, and varicella. The first vaccine dose is recommended at age 12 to 15 months and the second at age 4 to 6 years.

Consistent with ACIP General Recommendations on Immunization, the 2007 ACIP recommendations for prevention of varicella included a preference for use of combination MMRV vaccine over separate injections of equivalent component vaccines (i.e., MMR vaccine and varicella vaccine). At its February 27, 2008, meeting, ACIP considered the preliminary results from the Vaccine Safety Datalink (VSD) and Merck studies, which suggested an increased risk for febrile seizures after the first dose of MMRV vaccine. Given the availability of alternative options for vaccination against measles, mumps, rubella, and varicella and the limited supply of MMRV vaccine, ACIP voted to change the preference language for MMRV vaccine to read as follows: "Combination MMRV vaccine is approved for use among healthy children aged 12 months--12 years. MMRV vaccine is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella. ACIP does not express a preference for use of MMRV vaccine over separate injections of equivalent component vaccines (i.e., MMR vaccine and varicella vaccine)." ACIP also recommended establishing a work group to conduct in-depth evaluation of the findings regarding the increased risk for febrile seizures after the first dose of MMRV vaccine to present for consideration of future policy options. CDC, FDA, and ACIP will communicate updates and implement further necessary actions based on these evaluations.

Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at http://www.vaers.hhs.gov or by telephone, 800-822-7967. Additional information on MMRV vaccine and febrile

seizures is available at http://www.cdc.gov/od/science/iso/vsd/mmrv.htm and http://www.fda.gov/cber/label/proquadlbinfo.htm.

2006 Guideline

Note from the National Guideline Clearinghouse and the Centers for Disease Control and Prevention (CDC): This guideline is a revision of General Recommendations on Immunization and updates the 2002 statement by the Advisory Committee on Immunization Practices (ACIP) (CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices and the American Academy of Family Physicians. MMWR 2002;51[No. RR-2]). This report is intended to serve as a general reference on vaccines and immunization. The principal changes include 1) expansion of the discussion of vaccination spacing and timing; 2) an increased emphasis on the importance of injection technique/age/body mass in determining appropriate needle length; 3) expansion of the discussion of storage and handling of vaccines, with a table defining the appropriate storage temperature range for inactivated and live vaccines; 4) expansion of the discussion of altered immunocompetence, including new recommendations about use of live-attenuated vaccines with therapeutic monoclonal antibodies; and 5) minor changes to the recommendations about vaccination during pregnancy and vaccination of internationally adopted children, in accordance with new ACIP vaccine-specific recommendations for use of inactivated influenza vaccine and hepatitis B vaccine. The most recent ACIP recommendations for each specific vaccine should be consulted for comprehensive discussion. This report, ACIP recommendations for each vaccine, and other information about vaccination can be accessed at CDC's National Center for Immunization and Respiratory Diseases (proposed) (formerly known as the National Immunization Program) Web site.

Timing and Spacing of Immunobiologics

General Principles for Vaccine Scheduling

Optimal response to a vaccine depends on multiple factors, including the nature of the vaccine and the age and immune status of the recipient. Recommendations for the age at which vaccines are administered are influenced by age-specific risks for disease, age-specific risks for complications, ability of persons of a certain age to respond to the vaccine, and potential interference with the immune response by passively transferred maternal antibody. Vaccines are recommended for members of the youngest age group at risk for experiencing the disease for whom efficacy and safety have been demonstrated.

Certain products, including inactivated vaccines, toxoids, recombinant subunit, and polysaccharide conjugate vaccines, require administering 2 or more doses for development of an adequate and persisting antibody response. Tetanus and diphtheria toxoids require periodic reinforcement or booster doses to maintain protective antibody concentrations. Unconjugated polysaccharide vaccines do not induce T-cell memory, and booster doses are not expected to produce substantially increased protection. Conjugation with a protein carrier improves the effectiveness of polysaccharide vaccines by inducing T-cell--dependent immunologic function. Vaccines that stimulate both cell-mediated immunity and neutralizing antibodies (e.g., live attenuated virus vaccines) usually can induce

prolonged immunity, even if antibody titers decline over time. Subsequent exposure to infection usually does not lead to viremia but to a rapid anamnestic antibody response.

Approximately 90 to 95% of recipients of a single dose of certain live vaccines administered by injection at the recommended age (i.e., measles, rubella, and yellow fever), have protective antibody (generally within 2 weeks of the dose). However, because a limited proportion of recipients (5 to 15%) of measles-mumps-rubella (MMR) or varicella vaccine fail to respond to 1 dose, a second dose is recommended to provide another opportunity to develop immunity. The majority of persons who fail to respond to the first dose of MMR or varicella vaccine respond to a second dose.

The Recommended Childhood and Adolescent Immunization Schedule and the Recommended Adult Immunization Schedule are revised annually. Physicians and other health-care providers should ensure that they are following the most up-to-date schedules, which are available from CDC's National Center for Immunization and Respiratory Diseases (proposed) Web site.

Spacing of Multiple Doses of the Same Antigen

Vaccination providers should adhere as closely as possible to the recommended childhood vaccination schedule. Recommended ages and intervals between doses of multidose antigens provide optimal protection or have the best evidence of efficacy. Recommended vaccines and recommended intervals between doses are provided in the original guideline document and in Table 1 below.

In certain circumstances, administering doses of a multidose vaccine at shorter than the recommended intervals might be necessary. This can occur when a person is behind schedule and needs to be brought up-to-date as quickly as possible or when international travel is impending. In these situations, an accelerated schedule can be implemented that uses intervals between doses shorter than those recommended for routine vaccination. Although the effectiveness of all accelerated schedules has not been evaluated in clinical trials, the Advisory Committee on Immunization Practices (ACIP) believes that when accelerated intervals are used the immune response is acceptable and will lead to adequate protection. The accelerated or minimum, intervals and ages that can be used for scheduling catch-up vaccinations are provided in Table 1 below. Vaccine doses should not be administered at intervals less than these minimum intervals or earlier than the minimum age. (**Note**: During measles outbreaks, if cases are occurring among infants aged <12 months, measles vaccination of infants as young as 6 months can be undertaken as an outbreak control measure. However, doses administered at ages <12 months should not be counted as part of the series [**Source**: CDC. Measles, mumps, and rubella vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1998;47(No. RR-8)])

In clinical practice, vaccine doses occasionally are administered at intervals less than the minimum interval or at ages younger than the minimum age. Doses administered too close together or at too young an age can lead to a suboptimal immune response. However, administering a dose a limited number of days

earlier than the minimum interval or age is unlikely to have a substantially negative effect on the immune response to that dose. Therefore, ACIP recommends that vaccine doses administered 4 or fewer days before the minimum interval or age be counted as valid. (**Note**: In certain situations, local or state requirements might mandate that doses of selected vaccines be administered on or after specific ages. For example, a school entry requirement might not accept a dose of MMR or varicella vaccine administered before the child's first birthday. ACIP recommends that physicians and other health-care providers comply with local or state vaccination requirements when scheduling and administering vaccines.) However, because of its unique schedule, this recommendation does not apply to rabies vaccine. Doses administered 5 or more days earlier than the minimum interval or age of any vaccine should not be counted as valid doses and should be repeated as age-appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval (Table 1 below). For example, if *Haemophilus influenzae* type b (Hib) doses one and two were administered only 2 weeks apart, because the minimum interval from dose one to dose two is 4 weeks, dose two is invalid and should be repeated. The repeat dose should be administered 4 or more weeks after the invalid (second) dose. The repeat dose would be counted as the second valid dose. Doses administered 5 or more days before the minimum age should be repeated on or after the child reaches the minimum age and 4 or more weeks after the invalid dose. For example, if the first dose of varicella vaccine were administered at age 10 months, the repeat dose would be administered no earlier than the child's first birthday. If the first dose of varicella vaccine were administered at age 11 months and 2 weeks, the repeat dose could be administered 2 weeks after the first birthday.

Certain vaccines produce increased rates of local or systemic reactions in certain recipients when administered too frequently (e.g., adult tetanus-diphtheria toxoid [Td]; pediatric diphtheria-tetanus toxoid [DT]; tetanus toxoid; and tetanus, reduced diphtheria acellular pertussis vaccine for adolescents and adults). Such reactions might result from the formation of antigen-antibody complexes. Optimal record keeping, maintaining patient histories, and adhering to recommended schedules can decrease the incidence of such reactions without adversely affecting immunity.

Table 1. Recommended and Minimum Ages and Intervals Between Vaccine Doses of Routinely Recommended Vaccines*

Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended Interval to next dose	Minimum Interval to next dose
Hepatitis B (HepB)-1[+]	Birth	Birth	1 to 4 mos	4 wks
HepB-2	1 to 2 mos	4 wks	2 to 17 mos	8 wks
HepB-3[&]	6 to 18 mos	24 wks	—	—
Diphtheria–tetanus-acellular pertussis (DTaP)-1[+]	2 mos	6 wks	2 mos	4 wks

Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended Interval to next dose	Minimum Interval to next dose
DTaP-2	4 mos	10 wks	2 mos	4 wks
DTaP-3	6 mos	14 wks	6 to 12 mos[$]	6 mos[$]**
DTaP-4	15 to 18 mos	12 mos	3 yrs	6 mos[$]
DTaP-5	4 to 6 yrs	4 yrs	—	—
Haemophilus influenzae type b (Hib)-1[+, ++]	2 mos	6 wks	2 mos	4 wks
Hib-2	4 mos	10 wks	2 mos	4 wks
Hib-3[&&]	6 mos	14 wks	6 to 9 mos[$]	8 wks
Hib-4	12 to 15 mos	12 mos	—	—
Inactivated poliovirus (IPV)-1[+]	2 mos	6 wks	2 mos	4 wks
IPV-2	4 mos	10 wks	2 to 14 mos	4 wks
IPV-3	6 to 18 mos	14 wks	3 to 5 yrs	4 wks
IPV-4	4 to 6 yrs	18 wks	—	—
Pneumococcal conjugate (PCV)-1[++]	2 mos	6 wks	2 mos	4 wks
PCV-2	4 mos	10 wks	2 mos	4 wks
PCV-3	6 mos	14 wks	6 mos	8 wks
PCV-4	12 to 15 mos	12 mos	—	—
Measles-mumps-rubella (MMR)-1[$]	12 to 15 mos	12 mos	3 to 5 yrs	4 wks
MMR-2[$]	4 to 6 yrs	13 mos	—	—
Varicella (Var)-1[$]	12 to 15 mos	12 mos	3 to 5 yrs	12 wks***
Var-2[$]	4 to 6 yrs	15 mos	—	—
Hepatitis A (HepA)-1[+]	12 to 23 mos	12 mos	6 to 18 mos[$]	6 mos[$]
HepA-2	18 to 41 mos	18 mos	—	—
Influenza inactivated[+++]	6 to 59 mos	6 mos[&&&]	1 mo	4 wks
Influenza live attenuated[+++]	—	5 yrs	6 to 10 wks	6 wks
Meningococcal conjugate[+]	11 to 12 yrs	11 yrs	—	—
Meningococcal polysaccharide (MPSV)-1	—	2 yrs	5 yrs[$]	5 yrs[$]

Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended Interval to next dose	Minimum Interval to next dose
MPSV-2[****]	—	7 yrs	—	—
Tetanus-diphtheria	11 to 12 yrs	7 yrs	10 yrs	5 yrs
Tetanus-diphtheria acellular pertussis (Tdap)[++++]	≥11 yrs	10 yrs	—	—
Pneumococcal polysaccharide (PPV)-1	—	2 yrs	5 yrs	5 yrs
PPV-2[&&&&]	—	7 yrs	—	—
Human papillomavirus (HPV)-1[$]	11 to 12 yrs	9 yrs	2 mos	4 weeks
HPV-2	11 to 12 yrs (+2 mos)	109 mos	4 mos	12 wks
HPV-3	11 to 12 yrs (+6 mos)	112 mos	—	—
Rotavirus (RV)-1[*****]	2 mos	6 wks	2 mos	4 wks
RV-2	4 mos	10 wks	2 mos	4 wks
RV-3	6 mos	14 wks	—	—
Zoster[+++++]	60 yrs	60 yrs	—	—

* Combination vaccines are available. Use of licensed combination vaccines is preferred over separate injections of their equivalent component vaccines (**Source**: CDC. Combination vaccines for childhood immunization: recommendations of the Advisory Committee on Immunization Practices [ACIP], the American Academy of Pediatrics [AAP], and the American Academy of Family Physicians [AAFP]. MMWR 1999;48[No. RR-5]). When administering combination vaccines, the minimum age for administration is the oldest age for any of the individual components; the minimum interval between doses is equal to the greatest interval of any of the individual components.

[+] Combination vaccines containing the Hepatitis B component are available-(HepB-Hib, DTaP-HepB-IPV, and HepA-HepB). These vaccines should not be administered to infants aged <6 weeks because of the other components (i.e., Hib, DTaP, HepA, and IPV).

[&] HepB-3 should be administered at least 8 weeks after HepB-2 and at least 16 weeks after HepB-1 and should not be administered before age 24 weeks.

[$] Calendar months.

** The minimum recommended interval between DTaP-3 and DTaP-4 is 6 months. However, DTaP-4 need not to be repeated if administered at least 4 months after DTaP-3.

++ For Hib and PCV, children receiving the first dose of vaccine at age ≥7 months require fewer doses to complete the series (**Source**: CDC. Recommended childhood and adolescent immunization schedule—United States, 2006. MMWR 2005; 54 [Nos. 51 & 52]:Q1-Q4).

&& If polyribosylribitol phosphate-meningococcal outer membrane protein (PRP-OMP) (Pedvax-Hib®, Merck Vaccine Division) was administered at age 2 and 4 months, a dose at age 6 months is not required.

$$ Combination measles-mumps-rubella-varicella (MMRV) vaccine can be used for children aged 12 months–12 years.

*** The minimum interval from VAR-1 to VAR-2 for persons beginning the series at age ≥13 years is 4 weeks.

+++ Two doses of influenza vaccine are recommended for children aged <9 years who are receiving the vaccine for the first time. Children aged <9 years who have previously received influenza vaccine and persons aged ≥9 years require only one dose per influenza season.

&&& The minimum age for inactivated influenza vaccine varies by vaccine manufacturer. Only Fluzone (manufactured by sanofi pasteur) is approved for children aged 6 to 35 months. The minimum age for Fluvirin (manufactured by Novartis) is 4 years. For Fluarix and FluLeval (manufactured by GlaxoSmithKline), the minimum age is 18 years.

$$$ Certain experts recommend a second dose of MPSV 3 years after the first dose for persons at increased risk for meningococcal disease.

**** A second dose of meningococcal vaccine is recommended for persons previously vaccinated with MPSV who remain at high risk for meningococcal disease. Meningococcal conjugate vaccine (MCV4) is preferred when revaccinating persons aged 11–55 years, but a second dose of MPSV is acceptable. (**Source**: CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2005;54[No. RR-7]).

++++ Only 1 dose of Tdap is recommended. Subsequent doses should be administered as Td. If vaccination to prevent tetanus and/or diphtheria disease is required for children aged 7–9 years, Td should be administered (minimum age for Td is 7 years). For one brand of Tdap, the minimum age is 11 years. The preferred interval between Tdap and a previous dose of Td is 5 years. In persons who have received a primary series of tetanus-toxoid–containing vaccine, for management of a tetanus-prone wound, the minimum interval after a previous dose of any tetanus-containing vaccine is 5 years.

&&&& A second dose of PPV is recommended for persons at highest risk for serious pneumococcal infection and those who are likely to have a rapid decline in pneumococcal antibody concentration. Revaccination 3 years after the previous dose can be considered for children at highest risk for severe pneumococcal infection who would be aged <10 years at the time of revaccination (**Source**: CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1997;46[No. RR-8]).

$$$$ HPV is approved for females aged 9 to 26 years.

***** The first dose of RV must be administered at age 6 to 12 weeks. The vaccine series should not be started at age ≥13 weeks. RV should not be administered to children aged ≥33 weeks regardless of the number of doses received at age 6 to 32 weeks.

+++++ Herpes zoster vaccine is approved as a single dose for persons who are aged ≥60 years with a history of varicella.

Simultaneous Administration

Experimental evidence and extensive clinical experience provide the scientific basis for administering vaccines simultaneously (i.e., during the same office visit, not combined in the same syringe). Simultaneously administering all vaccines for which a person is eligible is critical, including for childhood vaccination programs, because simultaneous administration increases the probability that a child will be vaccinated fully at the appropriate age. A study conducted during a measles outbreak demonstrated that approximately one third of measles cases among unvaccinated but vaccine-eligible preschool children could have been prevented if MMR had been administered at the same visit when another vaccine was administered. Simultaneous administration also is critical when preparing for foreign travel and/or if uncertainty exists that a person will return for further doses of vaccine.

Simultaneously administering the most widely used live and inactivated vaccines have produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately. Routinely administering all age-appropriate doses of vaccines simultaneously is recommended for children for whom no specific contraindications exist at the time of the visit. Administering combined MMR (or measles-mumps-rubella-varicella [MMRV] vaccine) yields safety and immunogenicity results similar to administering individual measles, mumps, and rubella vaccines at different sites. Therefore, no medical basis exists for administering these vaccines separately for routine vaccination instead of the preferred MMR combined vaccine. Administering separate antigens would result in a delay in protection for the deferred components. Response to MMR and varicella vaccines administered on the same day is identical to vaccines administered a month apart, and administration of MMRV combined vaccine is similar to administration of MMR and varicella vaccines on the same day. No evidence exists that oral rotavirus vaccine (RV) interferes with live vaccines administered by injection or intranasally (e.g., MMR and live-attenuated influenza vaccine [LAIV]). RV can be administered simultaneously or at any interval before or after injectable or intranasal live vaccines. No data exist about the immunogenicity of oral Ty21a typhoid vaccine when administered

concurrently or within 30 days of live virus vaccines. In the absence of such data, if typhoid vaccination is warranted, administration should not be delayed because of administration of live-attenuated virus vaccines.

Simultaneously administering pneumococcal polysaccharide vaccine (PPV) and inactivated influenza vaccine elicits a satisfactory antibody response without increasing the incidence or severity of adverse reactions. Simultaneously administering PPV and inactivated influenza vaccine is recommended for all persons for whom both vaccines are indicated.

Hepatitis B vaccine (HepB) administered with yellow fever vaccine is as safe and immunogenic as when these vaccines are administered separately. Measles and yellow fever vaccines have been administered safely at the same visit and without reduction of immunogenicity of each of the components.

Depending on vaccines administered in the first year of life, children aged 12 to 15 months might receive up to nine injections during a single visit (MMR, varicella, Hib, pneumococcal conjugate, DTaP, IPV, HepA, HepB, and influenza [seasonal] vaccines). To reduce the number of injections at the 12 to 15-month visit, the IPV and HepB series can be expedited and completed before the child's first birthday. MMRV can be administered as soon as possible on or after the first birthday and the fourth dose of DTaP administered at age 15 months. The majority of children aged 1 year who have received 2 (PRP-OMP) or 3 (PRP-tetanus [PRP-T], diphtheria CRM197 [CRM, cross-reactive material] protein conjugate [HbOC]) previous doses of Hib vaccine, and 3 previous doses of DTaP and PCV have had protection. The third (PRP-OMP) or fourth (PRP-T, HbOC) dose of the Hib series, and the fourth doses of DTaP and PCV are critical in boosting antibody titer and ensuring continued protection. However, the booster dose of the pneumococcal conjugate series can be deferred until age 15 to 18 months for children who are likely to return for future visits. The fourth dose of DTaP is recommended at age 15 to 18 months, but can be administered as early as age 12 months under certain circumstances. For infants at low risk for infection with hepatitis B virus (i.e., the mother tested negative for hepatitis B surface antigen [HBsAg] at the time of delivery), the HepB series can be completed at any time during ages 6 to 18 months. With use of certain HepB combination vaccines (i.e., combination Hib-HepB vaccine), the minimum age of administration of the final dose is 12 months because of the minimum age requirement for the last dose of the Hib series. Recommended spacing of doses should be maintained (see Table 1).

Use of combination vaccines can reduce the number of injections required at an office visit. Licensed combination vaccines can be used whenever any components of the combination are indicated and its other components are not contraindicated and if licensed by the Food and Drug Administration (FDA) for that dose in the series. Use of licensed combination vaccines is preferred to separate injection of their equivalent component vaccines to reduce the number of injections and missed opportunities to protect through vaccination. Only combination vaccines licensed by FDA should be used. Individual vaccines must never be mixed in the same syringe unless they are approved specifically for mixing by FDA. Only one vaccine (DTaP and PRP-T Hib vaccine, marketed as TriHIBit® [manufactured by sanofi pasteur]) is licensed by FDA for mixing in the same syringe. This vaccine should not be used for primary vaccination in infants aged 2, 4, and 6 months,

but it can be used as the last dose of the Hib vaccine series on or after age 12 months.

Nonsimultaneous Administration

No evidence exists that inactivated vaccines interfere with the immune response to other inactivated vaccines or to live vaccines. An inactivated vaccine can be administered either simultaneously or at any time before or after a different inactivated vaccine or live vaccine (see Table 2 in the original guideline document).

Data are limited concerning interference between live vaccines. The immune response to one live-virus vaccine might be impaired if administered within 30 days of another live-virus vaccine.

To minimize the potential risk for interference, injectable or nasally administered live vaccines not administered on the same day should be administered >4 weeks apart whenever possible (see Table 2 in the original guideline document). If injectable or nasally administered live vaccines are separated by <4 weeks, the vaccine administered second should not be counted as a valid dose and should be repeated. The repeat dose should be administered >4 weeks after the last invalid dose. Yellow fever vaccine can be administered at any time after single-antigen measles vaccine. Oral vaccines (Ty21a typhoid vaccine and RV) can be administered simultaneously or at any interval before or after other live vaccines (injectable or intranasal), if indicated.

Spacing of Antibody-Containing Products and Vaccines

Live Vaccines

Ty21a typhoid, yellow fever, and LAIV vaccines can be administered at any time before, concurrent with, or after administering any immune globulin, hyperimmune globulin, or intravenous immune globulin (IGIV). Blood (e.g., whole blood, packed red blood cells, and plasma) and other antibody-containing blood products (e.g., immune globulin, hyperimmune globulin, and IGIV) can inhibit the immune response to measles and rubella vaccines for 3 or more months. The effect of blood and immune globulin preparations on the response to mumps and varicella vaccines is unknown, but commercial immune globulin preparations contain antibodies to these viruses. Blood products available in the United States are unlikely to contain a substantial amount of antibody to yellow fever vaccine virus. The length of time that interference with injectable live vaccination (except yellow fever vaccine) can persist after the antibody-containing product is a function of the amount of antigen-specific antibody contained in the product. Therefore, after an antibody-containing product is received, live vaccines (except yellow fever vaccine, oral Ty21a typhoid vaccine, and LAIV) should be delayed until the passive antibody has degraded (see Table 3 in the original guideline document). If a dose of injectable live-virus vaccine (except yellow fever vaccine) is administered after an antibody-containing product but at an interval shorter than recommended in this guideline, the vaccine dose should be repeated unless serologic testing is feasible and indicates a response to the vaccine. The repeat dose or serologic testing should be performed after the interval indicated for the antibody-containing product (see Table 4 in the original guideline document).

See the original guideline document for more information about potential interactions between live vaccines and antibody containing products.

Inactivated Vaccines

Antibody-containing products interact less with inactivated vaccines, toxoids, recombinant subunit, and polysaccharide vaccines than with live vaccines. Therefore, administering inactivated vaccines and toxoids either simultaneously with or at any interval before or after receipt of an antibody-containing product should not substantially impair development of a protective antibody response. The vaccine or toxoid and antibody preparation should be administered at different sites by using the standard recommended dose. Increasing the vaccine dose volume or number of vaccinations is not indicated or recommended.

Interchangeability of Vaccines from Different Manufacturers

Certain vaccines are available from different manufacturers, and these vaccines usually are not identical in antigen content or amount or method of formulation. Manufacturers use different production processes, and their products might contain different concentrations of antigen per dose or a different stabilizer or preservative.

See the original guideline document for more information about interchangeability of Hib conjugate, HepB, HepA, and acellular pertussis vaccines from different manufacturers.

Lapsed Vaccination Schedule

Vaccination providers should administer vaccines as close to the recommended intervals as possible. However, longer-than-recommended intervals between doses do not reduce final antibody concentrations, although protection might not be attained until the recommended number of doses has been administered. With the exception of oral typhoid vaccine, an interruption in the vaccination schedule does not require restarting the entire series of a vaccine or toxoid or the addition of extra doses.

Unknown or Uncertain Vaccination Status

Vaccination providers frequently encounter persons who do not have adequate documentation of vaccinations. Providers should only accept written, dated records as evidence of vaccination. With the exception of influenza vaccine and PPV, self-reported doses of vaccine without written documentation should not be accepted. Although vaccinations should not be postponed if records cannot be found, an attempt to locate missing records should be made by contacting previous health-care providers reviewing state or local immunization information systems (IIS), and searching for a personally held record. If records cannot be located, these persons should be considered susceptible and should be started on the age-appropriate vaccination schedule. Serologic testing for immunity is an alternative to vaccination for certain antigens (e.g., measles, rubella, hepatitis A, and tetanus).

Contraindications and Precautions

Contraindications and precautions to vaccination dictate circumstances when vaccines will not be administered. The majority of precautions are temporary, and the vaccination can be administered later. A contraindication is a condition in a recipient that increases the risk for a serious adverse reaction. A vaccine should not be administered when a contraindication is present. For example, administering influenza vaccine to a person with an anaphylactic allergy to egg protein could cause serious illness in or death of the recipient.

National standards for pediatric vaccination practices have been established and include true contraindications and precautions to vaccination (see Table 5 in the original guideline document). The only contraindication applicable to all vaccines is a history of a severe allergic reaction after a previous dose of vaccine or to a vaccine constituent (unless the recipient has been desensitized). In addition, severely immunocompromised persons should generally not receive live vaccines. Children who experience encephalopathy within 7 days after administration of a previous dose of diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP), DTaP, or Tdap not attributable to another identifiable cause should not receive further doses of a vaccine that contains pertussis. Because of the theoretical risk for the fetus, women known to be pregnant should not receive live attenuated virus vaccines.

A precaution is a condition in a recipient that might increase the risk for a serious adverse reaction or that might compromise the ability of the vaccine to produce immunity (e.g., administering measles vaccine to a person with passive immunity to measles from a blood transfusion). A person might experience a more severe reaction to the vaccine than would have otherwise been expected; however, the risk for this happening is less than expected with a contraindication. In general, vaccinations should be deferred when a precaution is present. However, a vaccination might be indicated in the presence of a precaution because the benefit of protection from the vaccine outweighs the risk for an adverse reaction. For example, caution should be exercised in vaccinating a child with DTaP who, within 48 hours of receipt of a previous dose of DTP or DTaP, experienced fever >104 degrees F (>40.5 degrees C); had persistent, inconsolable crying for 3 or more hours; collapsed or experienced a shock-like state; or had a seizure <3 days after receiving the previous dose of DTP or DTaP. However, administering a pertussis-containing vaccine should be considered if the risk for pertussis is increased (e.g., during a pertussis outbreak). These precautions do not apply to administration of tetanus-reduced-diphtheria-acellular-pertussis vaccine for adolescents and adults. The presence of a moderate or severe acute illness with or without a fever is a precaution to administration of all vaccines. (See Table 5 in the original guideline document.)

See the original guideline document for further information about contraindications and precautions to vaccination.

Vaccine Administration

Infection Control and Sterile Technique

Persons administering vaccines should follow appropriate precautions to minimize risk for spread of disease. Hands should be cleansed with an alcohol-based waterless antiseptic hand rub or washed with soap and water between each patient contact. Occupational Safety and Health Administration (OSHA) regulations do not require gloves to be worn when administering vaccinations, unless persons administering vaccinations are likely to come into contact with potentially infectious body fluids or have open lesions on their hands. Needles used for injections must be sterile and disposable to minimize the risk for contamination. A separate needle and syringe should be used for each injection. Changing needles between drawing vaccine from a vial and injecting it into a recipient is not necessary. Different vaccines should never be mixed in the same syringe unless specifically licensed for such use, and no attempt should be made to transfer between syringes.

To prevent inadvertent needle-stick injury or reuse, needles and syringes should be discarded immediately after use in labeled, puncture-proof containers located in the same room where the vaccine is administered. Needles should not be recapped before being placed in the container. Safety needles or needle-free injection devices should be used if available to reduce the risk for injury.

Injection Route and Injection Site

With the exception of Bacillus Calmette-Guerin (BCG) vaccine, injectable vaccines are administered by the intramuscular and subcutaneous route. The method of administration of injectable vaccines is determined, in part, by the presence of adjuvants in some vaccines. The term adjuvant refers to a vaccine component distinct from the antigen that enhances the immune response to the antigen. The majority of vaccines containing an adjuvant (e.g., DTaP, DT, Td, Tdap, PCV, Hib, HepA , HepB, and HPV) should be injected into a muscle because administration subcutaneously or intradermally can cause local irritation, induration, skin discoloration, inflammation, and granuloma formation. Anthrax vaccine, an inactivated vaccine with adjuvant, is an exception to this rule and is recommended to be administered subcutaneously. Routes of administration are recommended by the manufacturer for each immunobiologic (see Table 6 in the original guideline document). Deviation from the recommended route of administration might reduce vaccine efficacy or increase local adverse reactions.

Intramuscular Injections and Needle Length

Injectable immunobiologics should be administered where local, neural, vascular, or tissue injury is unlikely. Use of longer needles has been associated with less redness or swelling than occurs with shorter needles because of injection into deeper muscle mass. Appropriate needle length depends on age and body mass.

For all intramuscular injections, the needle should be long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underlying nerves, blood vessels, or bone. Vaccinators should be familiar with the anatomy of the area into which they are injecting vaccine. Intramuscular injections are administered at a 90-degree angle to the skin, preferably into the anterolateral aspect of the thigh or the deltoid muscle of the upper arm, depending on the age of the patient (see Table 7 in the original guideline document).

Decision on needle size and site of injection must be made for each person on the basis of the size of the muscle, the thickness of adipose tissue at the injection site, the volume of material to be administered, injection technique, and the depth below the muscle surface into which the material is to be injected (see Figure 1 in the original guideline document). Aspiration before injection of vaccines or toxoids (i.e., pulling back on the syringe plunger after needle insertion, before injection) is not required because no large blood vessels exists at the recommended injection sites.

See the original guideline document for specific recommendations on injection location and needle size for infants (aged <12 months), toddlers and older children (aged 12 months to 10 years), and adolescents and adults (aged ≥11 years).

Subcutaneous Injections

Subcutaneous injections are administered at a 45-degree angle usually into the thigh for infants aged <12 months and in the upper-outer triceps area of persons aged ≥12 months. Subcutaneous injections can be administered into the upper-outer triceps area of an infant, if necessary. A 5/8-inch, 23 to 25-gauge needle should be inserted into the subcutaneous tissue (see Figures 4 and 5 in the original guideline document).

Multiple Vaccinations

If multiple vaccines are administered at a single visit, administration of each preparation at a different anatomic site is desirable. For infants and younger children, if more than two vaccines must be injected in a single limb, the thigh is the preferred site because of the greater muscle mass; the injections should be sufficiently separated (i.e., 1 inch or more if possible) so that any local reactions can be differentiated. For older children and adults, the deltoid muscle can be used for more than one intramuscular injection. If a vaccine and an immune globulin preparation are administered simultaneously (e.g., Td/Tdap and tetanus immune globulin [TIG], HepB and hepatitis B immunoglobulin [HBIG]), separate anatomic sites should be used for each injection. The location of each injection should be documented in the patients' medical record.

Jet Injection

Jet injectors (JIs) are needle-free devices that drive liquid medication through a nozzle orifice, creating a narrow stream under high pressure that penetrates skin to deliver a drug or vaccine into intradermal, subcutaneous, or intramuscular tissues. JIs have the potential to reduce the frequency of needle-stick injuries to health-care workers and to overcome the improper reuse and other drawbacks of needles and syringes in economically developing countries. JIs have been safe and effective for administering different live and inactivated vaccines for viral and bacterial diseases. The immune responses generated are equivalent to, and occasionally greater than, immune responses induced by needle injection. However, local reactions or injury (e.g., redness, induration, pain, blood, and ecchymosis at the injection site) can be more frequent when vaccines are delivered by JIs compared with needle injection.

In the 1990s, a new generation of JIs was introduced with disposable cartridges serving as dose chambers and nozzle. With the provision of a new sterile cartridge for each patient and correct use, these devices avoid the safety concerns for multiple-use–nozzle devices. These devices should be used in accordance with their labeling for intradermal, subcutaneous, or intramuscular administration.

Methods for Alleviating Discomfort and Pain Associated with Vaccination

Comfort measures, such as distraction techniques (e.g., playing music or pretending to blow away the pain) ingestion of sweet liquids, breast feeding, cooling of the injection site, and topical or oral analgesia, can help infants or children cope with the discomfort associated with vaccination. Pretreatment (30–60 minutes before injection) with 5% topical lidocaine-prilocaine emulsion can decrease the pain of vaccination among infants by causing superficial anesthesia. Evidence indicates that this cream does not interfere with the immune response to MMR. Topical lidocaine-prilocaine emulsion should not be used on infants aged <12 months who are receiving treatment with methemoglobin-inducing agents because of the possible development of methemoglobinemia.

Acetaminophen has been used among children to reduce the discomfort and fever associated with DTP vaccination. However, acetaminophen can cause formation of methemoglobin and might interact with lidocaine-prilocaine cream, if used concurrently. Use of a topical refrigerant (vapocoolant) spray immediately before vaccination can reduce the short-term pain associated with injections and can be as effective as lidocaine-prilocaine cream.

Nonstandard Vaccination Practices

Recommendations regarding route, site, and dosage of immunobiologics are derived from data from clinical trials, from practical experience, and from theoretical considerations. ACIP discourages variations from the recommended route, site, volume, or number of doses of any vaccine.

See the original guideline document for further discussion of nonstandard vaccination practices.

Preventing Adverse Reactions

Vaccines are intended to produce active immunity to specific antigens. An adverse reaction is an untoward effect that occurs after a vaccination that is extraneous to the vaccine's primary purpose of producing immunity. Vaccine adverse reactions are classified by three general categories: local, systemic, and allergic. Local reactions are usually the least severe and most frequent. Systemic reactions (e.g., fever) occur less frequently than local reactions. Serious allergic reactions (e.g., anaphylaxis) are the most severe and least frequent. Severe adverse reactions are rare.

Persona who administers vaccines should screen their patients for contraindications and precautions to the vaccine before each dose of vaccine is administered (see Table 5 of the original guideline). Screening can be facilitated by consistent use of screening questionnaires, which are available from certain

state vaccination programs and other sources (e.g., the Immunization Action Coalition).

See the original guideline document for information on syncope.

Managing Acute Vaccine Reactions

Although rare after vaccination, the immediate onset and life-threatening nature of an anaphylactic reaction require that all personnel and facilities providing vaccinations have procedures in place for managing a reaction. All vaccine providers should be familiar with the office emergency plan and be certified in cardiopulmonary resuscitation. Epinephrine and equipment for maintaining an airway should be available for immediate use.

Anaphylaxis usually begins within minutes of vaccine administration. Rapidly recognizing and initiating treatment are required to prevent possible progression to cardiovascular collapse. If flushing, facial edema, urticaria, itching, swelling of the mouth or throat, wheezing, difficulty breathing, or other signs of anaphylaxis occur, the patient should be placed in a recumbent position with the legs elevated. Treatment options for management of anaphylaxis using pharmaceuticals have been recommended (see Table 8 in the original guideline document). Maintenance of an airway and oxygen administration might be necessary. Arrangements should be made for immediate transfer to an emergency facility for further evaluation and treatment.

Occupational Safety Regulations

Bloodborne diseases (e.g., hepatitis B and C and human immunodeficiency virus [HIV]) are occupational hazards for health-care workers. To reduce the incidence of needle-stick injury and the consequent risk for bloodborne diseases acquired from patients, the Needlestick Safety and Prevention Act was enacted in November 2000. The Act directed OSHA to strengthen its existing bloodborne pathogen standards.

See the original guideline document for additional information about the Act and OSHA standards. Additional information regarding implementation and enforcement of these regulations is available at the OSHA Web site.

Storage and Handling of Immunobiologics

Failure to adhere to recommended specifications for storage and handling of immunobiologics can reduce potency, resulting in an inadequate immune response in the recipient. Recommendations in the product package inserts, including methods for reconstitution of the vaccine, should be followed carefully. Vaccine quality is the shared responsibility of all handlers from the time the vaccine is manufactured until administration. All vaccines should be inspected upon delivery and monitored during storage to ensure that the cold chain has been maintained. Vaccines should continue to be stored at recommended temperatures immediately upon receipt until use.

For further information on storage and handling of immunobiologics, including storage temperature, temperature monitoring, response to out-of-temperature range storage, expiration dates and windows, multidose vials, and prefilling syringes, see the original guideline document.

Altered Immunocompetence

General Principles

Altered immunocompetence is a term often used synonymously with immunosuppression and immunocompromise that includes conditions commonly classified as primary immunodeficiency and secondary immunodeficiency.

Primary immunodeficiencies generally are inherited and include conditions defined by an absence or quantitative deficiency of cellular and/or humoral components that provide immunity. Examples include congenital immunodeficiency diseases (e.g., X-linked agammaglobulinemia), severe combined immunodeficiency disease, and chronic granulomatous disease. Secondary immunodeficiency generally is acquired and is defined by loss or qualitative deficiency in cellular and humoral immune components that occurs as a result of a disease process or its therapy. Examples of secondary immune deficiency include HIV infection, hematopoietic malignancies, treatment with radiation, and treatment with immunosuppressive drugs, including alkylating agents and antimetabolites. The degree to which immunosuppressive drugs cause clinically significant immunodeficiency generally is dose-related and varies by drug. Primary and secondary immunodeficiencies might display a combination of deficits in both cellular and humoral immunity. In this report, the general term altered immunocompetence also will be used to include conditions such as asplenia and chronic renal disease and treatments with therapeutic monoclonal antibodies (specifically the tumor-necrosis-factor alpha inhibitors) and prolonged high-dose corticosteroids.

Determination of altered immunocompetence is important to the vaccine provider because the incidence or severity of certain vaccine-preventable diseases is higher in persons with altered immunocompetence; therefore, certain vaccines (e.g., inactivated influenza and pneumococcal vaccines) are recommended specifically for persons with these diseases. Vaccines might be less effective during the period of altered immunocompetence. Live vaccines generally should be deferred until immune function has improved. Inactivated vaccines administered during the period of altered immunocompetence might need to be repeated after immune function has improved. Finally, persons with altered immunocompetence might be at increased risk for an adverse reaction after administration of live-attenuated vaccines because of reduced ability to mount an effective immune response.

The degree of altered immunocompetence in a patient should be determined by a physician. The challenge for clinicians and other health-care providers is in assessing the safety and effectiveness of vaccines for conditions associated with primary or secondary immunodeficiency, especially when new therapeutic modalities are being used and information about the safety and effectiveness of vaccines has not been characterized fully in persons receiving these drugs (see Table 11 in the original guideline document). Laboratory studies can be useful for assessing the effects of a disease or drug on the immune system. Tests useful to

assess humoral immunity include immunoglobulin (and immunoglobulin subset) levels and specific antibody levels (tetanus, diphtheria, and response to pneumococcal vaccine). Tests that demonstrate the status of cellular immunity include lymphocyte numbers (i.e., a complete blood count with differential), a test that delineates concentrations and proportions of lymphocyte subsets (i.e., B and T-lymphocytes, CD4+ versus CD8+ lymphocytes), and tests that measure T-lymphocyte proliferation in response to specific or nonspecific stimuli (e.g., lymphocyte proliferation assays). The ability to characterize a drug or disease condition as affecting cellular or humoral immunity is only the first step; using this information to draw inferences about whether particular vaccines are indicated or whether caution is advised with use of live or inactivated vaccines is more complicated and might require consultation with an infectious disease or immunology specialist.

Altered Immunocompetence as an Indication to Receive a Vaccine

Persons with altered immunocompetence generally are advised to receive TIV and polysaccharide-based vaccines (i.e., PCV, PPV, MCV4, MPSV, and Hib vaccines) on the basis of demonstrated effectiveness and an increased risk for disease if the vaccine is withheld.

See the original guideline document for specific recommendations about pneumococcal, influenza, meningococcal, and Hib vaccines in persons with altered immunocompetence, as well as information about vaccination of contacts of persons with altered immunocompetence, vaccination with inactivated vaccines, vaccination with live-attenuated vaccines, recipients of hematopoietic stem cell transplant, and situations in which some degree of immunodeficiency might be present.

Special Situations

Concurrently Administering Antimicrobial Agents and Vaccines

With limited exceptions, using an antibiotic is not a contraindication to vaccination. Antimicrobial agents have no effect on the response to live attenuated vaccines, except live oral Ty21a typhoid vaccine, and have no effect on inactivated, recombinant subunit, or polysaccharide vaccines or toxoids. Ty21a typhoid vaccine should not be administered to persons receiving antimicrobial agents until 24 hours after any antibiotic dose of antimicrobial agent.

Antiviral drugs used for treatment or prophylaxis of influenza virus infections have no effect on the response to inactivated influenza vaccine. However, live-attenuated influenza vaccine should not be administered until 48 hours after cessation of therapy using antiviral influenza drugs. If feasible, antiviral medication should not be administered for 2 weeks after LAIV administration. Antiviral drugs active against herpesviruses (e.g., acyclovir or valacyclovir) might reduce the efficacy of live-attenuated varicella vaccine. These drugs should be discontinued at least 24 hours before administration of varicella-containing vaccines, if possible.

The antimalarial drug mefloquine could affect the immune response to oral Ty21a typhoid vaccine if both are taken simultaneously. To minimize this effect,

administering Ty21a typhoid vaccine at least 24 hours before or after a dose of mefloquine is prudent.

Tuberculosis Screening and Skin Test Reactivity

Measles illness, severe acute or chronic infections, HIV infection, and malnutrition can create a relatively anergic state during which the tuberculin skin test (TST) (previously referred to as purified protein derivative [PPD] skin test) might give a false negative reaction. Although any live attenuated measles vaccine can theoretically suppress TST reactivity, the degree of suppression is probably less than that occurring from acute infection from wild-type measles virus. Although routine TST screening of all children is no longer recommended, TST screening is sometimes needed at the same time as administering a measles-containing vaccine (e.g., for well-child care, school entrance, or for employee health reasons).

TST and measles-containing vaccine can be administered at the same visit (preferred option). Simultaneously administering TST and measles-containing vaccine does not interfere with reading the TST result at 48 to 72 hours and ensures that the person has received measles vaccine.

If the measles-containing vaccine has been administered recently, TST screening should be delayed for at least 4 weeks after vaccination. A delay in performing TST will remove the concern of any theoretical but transient suppression of TST reactivity from the vaccine.

TST screening can be performed and read before administering the measles-containing vaccine. This option is the least favored because it will delay receipt of the measles-containing vaccine.

No data exist for the potential degree of TST suppression that might be associated with other injectable live-attenuated virus vaccines (e.g., varicella and yellow fever). However, in the absence of data, following guidelines for measles-containing vaccine when scheduling TST screening and administering other parenteral live attenuated virus vaccines is prudent. If the opportunity to vaccinate might be missed, vaccination should not be delayed only because of these theoretical considerations. Because of similar concerns about smallpox vaccine and TST suppression, a TST should not be performed until four weeks after smallpox vaccination.

TST reactivity in the absence of tuberculosis disease is not a contraindication to administration of any vaccine, including live-attenuated virus vaccines. Tuberculosis disease is not a contraindication to vaccination, unless the person is moderately or severely ill. Although no studies have reported the effect of MMR vaccine on persons with untreated tuberculosis, a theoretical basis exists for concern that measles vaccine might exacerbate tuberculosis. As a result, before administering MMR to persons with untreated active tuberculosis, initiating antituberculosis therapy is advisable. Considering if concurrent immunosuppression (e.g., immunosuppression caused by HIV infection) is a concern before administering live attenuated vaccines also is prudent.

Severe Allergy to Vaccine Components

Vaccine components can cause allergic reactions among certain recipients. These reactions can be local or systemic and can include mild-to-severe anaphylaxis or anaphylactic-like responses (e.g., generalized urticaria or hives, wheezing, swelling of the mouth and throat, difficulty breathing, hypotension, and shock). Allergic reactions might be caused by the vaccine antigen, residual animal protein, antimicrobial agents, preservatives, stabilizers, or other vaccine components. Components of each vaccine are listed in the perspective package insert. An extensive listing of vaccine components, their use, and the vaccines that contain each component has been published and is also available from the CDC's National Center for Immunization and Respiratory Diseases (proposed) Web site. See the original guideline document for a discussion of some of the common vaccine components and potential allergic reactions.

Latex Allergy

The most common type of latex sensitivity is contact-type (type 4) allergy, usually as a result of prolonged contact with latex-containing gloves. However, injection-procedure–associated latex allergies among patients with diabetes mellitus have been described. Allergic reactions (including anaphylaxis) after vaccination procedures are rare. Only one report of an allergic reaction after administering HepB to a patient with known severe allergy (anaphylaxis) to latex has been published.

If a person reports a severe (anaphylactic) allergy to latex, vaccines supplied in vials or syringes that contain natural rubber should not be administered, unless the benefit of vaccination outweighs the risk for potential allergic reaction. For latex allergies other than anaphylactic allergies (e.g., a history of contact allergy to latex gloves), vaccines supplied in vials or syringes that contain dry natural rubber or natural rubber latex can be administered.

Vaccination of Preterm Infants

In the majority of cases, infants born prematurely, regardless of birthweight, should be vaccinated at the same chronological age and according to the same schedule and precautions as full-term infants and children. Birthweight and size are not factors in deciding whether to postpone routine vaccination of a clinically stable preterm infant, except for HepB. The full recommended dose of each vaccine should be used. Divided or reduced doses are not recommended.

Decreased seroconversion rates might occur among certain preterm infants with low birthweights (i.e., <2,000 g) after administration of HepB at birth. However, by chronological age 1 month, all preterm infants, regardless of initial birth weight or gestational age are likely to respond as adequately as older and larger infants. Preterm infants born to HBsAg-positive mothers and mothers with unknown HBsAg status must receive immunoprophylaxis with HepB and hepatitis B immunoglobulin (HBIG) within 12 hours after birth. If these infants weigh <2,000 g at birth, the initial vaccine dose should not be counted towards completion of the HepB series, and 3 additional doses of HepB should be administered, beginning when the infant is aged 1 month. Preterm infants weighing <2,000 g and born to HBsAg-negative mothers should receive the first dose of the HepB series at chronological age 1 month or at hospital discharge.

Breast Feeding and Vaccination

Neither inactivated nor live vaccines administered to a lactating woman affect the safety of breast feeding for women or their infants. Breast feeding does not adversely affect immunization and is not a contraindication for any vaccine, with the exception of smallpox vaccine. Limited data indicate that breast feeding can enhance the response to certain vaccine antigens. Breast fed infants should be vaccinated according to recommended schedules.

Although live vaccines multiply within the mother's body, the majority have not been demonstrated to be excreted in human milk. Although rubella vaccine virus might be excreted in human milk, the virus usually does not infect the infant. If infection does occur, it is well-tolerated because the virus is attenuated. Inactivated, recombinant, subunit, polysaccharide, conjugate vaccines and toxoids pose no risk for mothers who are breast feeding or for their infants.

Vaccination During Pregnancy

Risk for a developing fetus from vaccination of the mother during pregnancy primarily is theoretical. No evidence exists of risk from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids. Live vaccines pose a theoretical risk to the fetus. Benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high, when infection would pose a risk to the mother or fetus, and when the vaccine is unlikely to cause harm.

See the original guideline document for specific recommendations for vaccination during pregnancy.

Persons Vaccinated Outside the United States, Including Internationally Adopted Children

The ability of a clinician to determine that a person is protected on the basis of their country of origin and their records alone is limited. Vaccines administered outside the United States can generally be accepted as valid if the schedule was similar to that recommended in the United States (i.e., minimum ages and intervals). Only written documentation should be accepted as evidence of previous vaccination. Written records are more likely to predict protection if the vaccines, dates of administration, intervals between doses, and the person's age at the time of vaccination are comparable to U.S. recommendations. Although vaccines with inadequate potency have been produced in other countries, the majority of vaccines used worldwide are produced with adequate quality control standards and are potent.

The number of U.S. families adopting children from outside the United States has increased substantially in recent years. Adopted children's birth countries often have vaccination schedules that differ from the recommended childhood immunization schedule in the United States. Differences in the U.S. immunization schedule and those used in other countries include the vaccines administered, the recommended ages of administration, and the number and timing of doses.

Data are inconclusive about the extent to which an internationally adopted child's immunization record reflects the child's protection. A child's record might indicate administration of MMR vaccine when only single-antigen measles vaccine was administered.

Clinicians and other health-care providers can follow one of multiple approaches if a question exists regarding whether vaccines administered to an international adoptee were immunogenic. Repeating the vaccinations is an acceptable option. Doing so is usually safe and avoids the need to obtain and interpret serologic tests. If avoiding unnecessary injections is desired, judicious use of serologic testing might be helpful in determining which immunizations are needed. For some vaccines, the most readily available serologic tests cannot document protection against infection. These recommendations provide guidance on possible approaches to evaluation and revaccination for each vaccine recommended universally for children in the United States (see Table 12 in the original guideline document). Clinicians and other health-care providers should ensure that household contacts of international adoptees are adequately vaccinated, particularly for measles and hepatitis B.

See the original guideline document for recommendations about specific vaccines, including MMR, Hib, HepA, HepB, IPV, DTaP, varicella, and pneumococcal vaccine.

Vaccinating Persons with Bleeding Disorders and Persons Receiving Anticoagulant Therapy

Because of the risk for hematoma formation after injections, intramuscular injections are often avoided among persons with bleeding disorders by using the subcutaneous or intradermal routes for vaccines that are administered normally by the intramuscular route.

When Hep B or any other intramuscular vaccine is indicated for a patient with a bleeding disorder or a person receiving anticoagulant therapy, the vaccine should be administered intramuscularly if, in the opinion of a physician familiar with the patient's bleeding risk, the vaccine can be administered with reasonable safety by this route. If the patient receives antihemophilia or similar therapy, intramuscular vaccinations can be scheduled shortly after such therapy is administered. A fine needle (23 gauge or smaller) should be used for the vaccination and firm pressure applied to the site, without rubbing, for at least 2 minutes. The patient or family should be instructed concerning the risk for hematoma from the injection.

Vaccination Records

See the original guideline document for information on consent to vaccinate, provider records, patients' personal records, and immunization information systems.

Reporting Adverse Events After Vaccination

Modern vaccines are safe and effective; however, adverse events have been reported after administration of all vaccines. These events range from frequent, minor, local reactions to extremely rare, severe, systemic illness (e.g.,

anaphylaxis). Establishing evidence for cause-and-effect relations on the basis of case reports and case series alone is impossible because temporal association alone does not necessarily indicate causation. Unless the syndrome that occurs after vaccination is clinically or pathologically distinctive, more detailed epidemiologic studies to compare the incidence of the event among vaccinees with the incidence among unvaccinated persons are often necessary. Reporting adverse events to public health authorities, including serious events, is a key stimulus to developing studies to confirm or refute a causal association with vaccination. More complete information regarding adverse reactions to a specific vaccine can be found in the ACIP recommendations for that vaccine and in a specific statement on vaccine adverse reactions.

The National Childhood Vaccine Injury Act requires health-care providers to report selected events occurring after vaccination to the Vaccine Adverse Event Reporting System (VAERS). Events for which reporting is required appear in the Reportable Events Table. (The Reportable Events Table can be obtained from the Vaccine Injury Compensation Program (VICP) Web site.)

Persons other than health-care providers to report selected events occurring after vaccination to VAERS. All clinically significant adverse events other than those that must be reported or that occur after administration of vaccines not covered by the Act should also be reported to VAERS, even if the physician or other health-care provider is uncertain they are related causally to vaccination. VAERS forms and instructions are available in the FDA Drug Bulletin, by contacting VAERS (800-822-7967), or from the VAERS Web site.

National Vaccine Injury Compensation Program

See the original guideline document for information about the National Vaccine Injury Compensation Program.

Benefit and Risk Communication

Parents, guardians, legal representatives, and adolescent and adult patients should be informed regarding the benefits and risks of vaccines in understandable language. Opportunity for questions should be provided before each vaccination. Discussion of the benefits of and risks for vaccination is sound medical practice and is required by law.

See the original guideline document for further discussion of benefit and risk communication.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

Vaccine recommendations are based on characteristics of the immunobiologic product, scientific knowledge about the principles of active and passive immunization, epidemiology and burden of diseases (i.e., morbidity, mortality, costs of treatment, and loss of productivity), vaccine safety considerations, costs analysis of preventive measures, published and unpublished studies, and expert opinion of public health officials and specialists in clinical and preventive medicine.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Benefits of vaccination include partial or complete protection against infection for the vaccinated person and overall benefits to society as a whole. Benefits include protection from symptomatic illness, improved quality of life and productivity, and prevention of death. Societal benefits include creation and maintenance of herd immunity against communicable diseases, prevention of disease outbreaks, and reduction in health-care-related costs.

POTENTIAL HARMS

- In general, vaccination risks range from common, minor, and local adverse effects to rare, severe, and life-threatening conditions.
- The immune response to one live-virus might be impaired if administered within 30 days of another live-virus vaccine.
- Local reactions or injury (e.g., redness, induration, pain, blood, and ecchymosis) can be more frequent when vaccines are delivered by jet injectors compared with needle injections.
- Acetaminophen can cause formation of methemoglobin and, thus, might interact with lidocaine-prilocaine cream, if used concurrently.
- Syncope (vasovagal or vasodepressor reaction) can occur after vaccination, most commonly among adolescents and young adults.
- Needle-stick injuries may occur among health-care workers, with the consequent risk for bloodborne diseases acquired from patients.
- Vaccine components can cause allergic reactions among certain recipients. These reactions can be local or systemic and can include mild to severe anaphylaxis or anaphylactic-like responses (e.g., generalized urticaria or hives, wheezing, swelling of the mouth and throat, difficulty breathing, hypotension, and shock).

2008 Addendum

The administration of the combination measles, mumps, rubella, and varicella (MMRV) vaccine is associated with risk for febrile seizures.

CONTRAINDICATIONS

CONTRAINDICATIONS

- The only true contraindication applicable to all vaccines is a history of a severe allergic reaction after a previous dose of vaccine or to a vaccine constituent (unless the recipient has been desensitized). In addition, severely immunocompromised persons should generally not receive live vaccines. Children who experience encephalopathy within 7 days after administration of a previous dose of diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP), diphtheria-tetanus-acellular pertussis vaccine (DTaP), or tetanus-diphtheria acellular pertussis vaccine (Tdap) not attributable to another identifiable cause should not receive further doses of a vaccine that contains pertussis. Because of the theoretical risk for the fetus, women known to be pregnant should generally not receive live-attenuated virus vaccines.
- See the "Major Recommendations" section of this summary and Table 5 of the original guideline document for a more complete discussion of contraindications and precautions to commonly used vaccines.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

To maximize the benefits of vaccination, this report provides general information about immunobiologics and provides practical guidelines about vaccine administration and technique. (The most recent Advisory Committee on Immunization Practices [ACIP] recommendations for each specific vaccine should be consulted for comprehensive discussion.) These recommendations are intended for use in the United States because vaccine availability and use and epidemiologic circumstances differ in other countries. Individual circumstances might warrant deviations from these recommendations. The relative balance of benefits and risks can change as diseases are controlled or eradicated.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Vaccination Programs

The best way to reduce vaccine-preventable diseases is to have a highly immune population. Universal vaccination is a critical part of quality health care and should be accomplished through routine and intensive vaccination programs implemented in physicians' offices and in public health clinics. Programs should be established and maintained in all communities to ensure vaccination of all children at the recommended age. In addition, appropriate vaccinations should be available for all adolescents and adults.

Physicians and other pediatric vaccination providers should adhere to the standards for child and adolescent vaccination practices. These standards define appropriate vaccination practices for both the public and private sectors. The standards provide guidance on practices that will result in eliminating barriers to vaccination. These include practices aimed at eliminating unnecessary prerequisites for receiving vaccinations, eliminating missed opportunities to vaccinate, improving procedures to assess vaccination needs, enhancing knowledge about vaccinations among parents and providers, and improving the

management and reporting of adverse events. In addition, the standards address the importance of recall and reminder systems and using assessments to monitor clinic or office vaccination coverage levels. Physicians and other health-care providers should simultaneously administer as many vaccine doses as possible, as indicated on the Recommended Child and Adolescent Immunization Schedule.

Standards of practice also have been published to increase vaccination coverage among adults. These standards include ensuring vaccine availability, routine review of vaccination status, communicating risks for and benefits to the patient, using standing orders, and recommending simultaneous administration of all indicated doses according to the Recommended Adult Immunization Schedule.

Every visit to a physician or other health-care provider can be an opportunity to update a patient's vaccination status with needed vaccinations. Official health agencies should take necessary steps, including when appropriate, developing and enforcing child care and school vaccination requirements, to ensure that students at all grade levels (including college) and children in day care centers are protected against vaccine-preventable diseases. Agencies also should encourage institutions (e.g., hospitals and long–term care facilities) to adopt policies about the appropriate vaccination of patients, residents, and employees.

Dates of vaccination (day, month, and year) should be recorded on institutional vaccination records (e.g., records kept in schools and day care centers). These records will facilitate assessments that a primary vaccination series has been completed according to an appropriate schedule and that needed booster doses have been administered at the appropriate time.

The independent, nonfederal Task Force on Community Preventive Services (the Task Force), whose membership is appointed by the Centers for Disease Control and Prevention (CDC), provides public health decision-makers with recommendations on population-based interventions to promote health and prevent disease, injury, disability, and premature death. The recommendations are based on systematic reviews of the scientific literature about effectiveness and cost-effectiveness of these interventions. In addition, the Task Force identifies critical information about the other effects of these interventions and the applicability to specific populations and settings and the potential barriers to implementation. This information is available at www.thecommunityguide.org.

See Table 13 in the original guideline document for a summary of recommendations for interventions to improve coverage of vaccines recommended for routine use among children, adolescents, and adults.

IMPLEMENTATION TOOLS

Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Safety
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

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GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

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GUIDELINE COMMITTEE

General Recommendations on Immunization Working Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The Centers for Disease Control and Prevention (CDC), their planners, and their presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

This report will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of the discussion of:

1. The nonsimultaneous administration of yellow fever vaccine and inactivated vaccines.
2. Progressive neurologic disorders are a precaution for the use of tetanus-reduced diphtheria acellular pertussis vaccine for adolescents and adults.
3. Contact allergy to latex is neither a contraindication nor a precaution to the use of meningococcal vaccine in the absence of an anaphylactic allergy.
4. Meningococcal conjugate vaccine should be administered intramuscularly, but if administered subcutaneously, repeating the dose is unnecessary.
5. Use of immune globulin, intravenous for postexposure prophylaxis or varicella.
6. Use of VariZIG for postexposure prophylaxis of varicella (unlicensed).

ENDORSER(S)

American Academy of Pediatrics - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Kroger AT, Atkinson WL, Marcuse EK, Pickering LK, Advisory Committee on Immunization Practices (ACIP) Centers for Disease. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP) [published errata appear in MMWR Morb Mortal Wkly Rep 2007 Mar 23;56(11):256]. MMWR Recomm Rep 2006 Dec 1;55(RR-15):1-48.

GUIDELINE AVAILABILITY

2006 Guideline

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site:

- HTML Format
- Portable Document Format (PDF)

Print copies: Available from the Centers for Disease and Control Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

2008 Addendum

Available from the Centers for Disease Control and Prevention (CDC Web site).

AVAILABILITY OF COMPANION DOCUMENTS

A Continuing Education activity is available from the Centers for Disease Control and Prevention (CDC) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 20, 2002. This summary was updated by ECRI on October 20, 2004 after the Centers for Disease Control and Prevention (CDC) issued interim recommendations in response to the shortage of influenza vaccine. This summary was updated again by ECRI on December 7, 2004. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on October 5, 2005 following the U.S. Food and Drug Administration (FDA) advisory on Menactra (Meningococcal Conjugate Vaccine A, C, Y, and W135). This summary was updated by ECRI on October 25, 2006 following the updated FDA advisory on Menactra (Meningococcal Conjugate Vaccine). This NGC summary was updated on January 2, 2007. This summary was updated by ECRI on February 19, 2007 following the FDA advisory on Rotavirus, Live, Oral, Pentavalent vaccine (RotaTeq). This summary was updated by ECRI Institute on July 9, 2007 following the FDA advisory on RotaTeq (Rotavirus, Live, Oral, Pentavalent) vaccine. This NGC summary was updated most recently by ECRI Institute on March 27, 2008.

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